Alvimopan (ENTEREG)

Criteria for Use

October 2016

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive alvimopan*

- ☐ Hypersensitivity to alvimopan or product components.
- ☐ Complete bowel obstruction or having surgery for correction of complete bowel obstruction
- ☐ Patients scheduled for total colectomy, ileostomy, colostomy, pancreatic anastomosis or gastric anastomosis. *For guidance regarding total abdominal hysterectomy, ileostomy and colostomy, see Issues for Consideration.*
- ☐ Inflammatory bowel disease
- ☐ Therapeutic doses of opioids for more than 7 consecutive days immediately prior to taking alvimopan
- ☐ Intrathecal or epidural opioids or anesthetics[1] are scheduled to be used during surgery
- ☐ Recent treatment with alvimopan in current episode of care (No studies evaluated safety and efficacy of more than one treatment course.)
- ☐ Situations where pre-operative dose cannot be administered
- ☐ Severe hepatic impairment (Child-Pugh C)
- ☐ Endstage renal disease
- ☐ Any non-FDA approved indication (E.A.S.E. program—see Entereg Ordering Instructions and VAMC Registration Form)

Inclusion Criteria *All of the following (A–B) must be fulfilled in order to meet criteria.*

Alvimopan is available only to hospitals that perform surgeries that include a bowel resection and is dispensed by pharmacies that are enrolled in the E.A.S.E. ENTEREG REMS Program.

- ☐ A. Undergoing surgery that includes partial bowel resection with primary anastomosis (including resection of intra-abdominal organs with large or small bowel resection / anastomoses, e.g. radical cystectomy)
- ☐ B. Intravenous postoperative opioid pain management is planned

** Particular consideration should be given to patients considered at risk for prolonged postoperative ileus (PPOI)

a. Prior occurrence of PPOI after any surgical procedure.
b. Anticipation of extensive (over 2 hours) adhesiolysis associated with a small or large bowel resection.
c. Significant en bloc resection of intra-abdominal organs including large or small bowel.

Dosage and Administration

- For hospital use only. The recommended adult dosage of alvimopan is 12 mg orally administered 30 minutes to 5 hours prior to surgery followed by 12 mg twice daily beginning the day after surgery until discharge for a maximum of 7 days. Patients should not receive more than 15 doses of alvimopan.
- No adjustments necessary for mild-moderate renal or hepatic disorder.

Monitoring

- Hemoglobin / Hematocrit – Consider monitoring for anemia.
- Potassium – Consider monitoring for hypokalemia.
- Signs and symptoms of urinary retention
- Closely monitor for possible adverse effects, such as cramping, diarrhea and gastrointestinal pain, in patients with mild to moderate hepatic or renal impairment and in Japanese patients. Discontinue treatment if adverse events occur. No dosage adjustment is required in these patients; however, the occurrence of adverse effects could indicate high drug or metabolite concentrations.

Issues for Consideration

FDA-approved Indication

- Alvimopan is an opioid antagonist indicated to accelerate the time to upper and lower gastrointestinal recovery following surgeries that include partial bowel resection with primary anastomosis.

BLACK BOX WARNING

- **Potential risk of myocardial infarction with long-term use: for short-term hospital use only.**

Warnings / Precautions

- Use caution in patients who received more than 3 doses of an opioid within the week prior to surgery. These patients may be at increased risk for gastrointestinal adverse effects such as abdominal pain, nausea, vomiting and diarrhea.
- Potential risk of myocardial infarction with long-term use. For short-term use (15 doses) through the E.A.S.E. program.

Pregnancy Category B

- No adequate and/or well-controlled studies in pregnant women.
- Use alvimopan during pregnancy only if clearly needed.

Types of Surgeries for Which Alvimopan Has Been Used

- Current evidence supports the use of alvimopan for in-hospital, open gastrointestinal surgery, radical cystectomy and total abdominal hysterectomy.[2,3,4]
- There have been three retrospective and two nonblinded prospective studies that might support *considering* the use of alvimopan for laparoscopic gastrointestinal surgery to reduce postoperative ileus.[5] Alvimopan improved the frequency of bowel function recovery but showed inconsistent effects on reduction in length of hospital stay and no effect on 30-day readmission rates. The magnitudes of these effects are likely to change with additional studies.
- Although major alvimopan clinical trials excluded patients with ileostomy, colostomy or other condition known or suspected to be associated with increased postoperative morbidity, other studies have included a small number of patients who had had ileostomy or colostomy or had surgery for ostomy reversal.[6] Alvimopan has also been used in patients undergoing total abdominal colectomy with ileostomy.[7] Cases that involve bowel resection with the addition of ostomy should not necessarily be excluded from the use of alvimopan, particularly in the presence of factors that increase the risk of prolonged postoperative ileus (e.g., case is long or requires extensive enterolysis / adhesiolysis). Ileostomy and colostomy may be considered relative contraindications to the use of alvimopan.

Renewal Criteria

- Maximum of 15 doses allowed
- Maximum of 7 days or until hospital discharge
- No renewal following the return of bowel function (i.e., bowel movement)
- No refills allowed

Revised: October 2016. Original April 2009. Contact: Francine Goodman, PharmD, BCPS, National Clinical Pharmacy Program Manager, VA Pharmacy Benefits Management Services

[1] McRae WH 3rd, Simpson-Camp L, Hammen PF, Al-Sayegh HK. The use of alvimopan in patients receiving epidural analgesia after large bowel resection. Am Surg. 2015 Feb;81(2):212-6

[2] Berger NG, Ridolfi TJ, Ludwig KA. Delayed gastrointestinal recovery after abdominal operation - role of alvimopan. Clin Exp Gastroenterol. 2015 Aug 5;8:231-5

[3] Cui Y, Chen H, Qi L, Zu X, Li Y. Effect of alvimopan on accelerates gastrointestinal recovery after radical cystectomy: A systematic review and meta-analysis. Int J Surg 2016; 25: 1–6

[4] Herzog TJ, Coleman RL, Guerrieri Jr JP, Gabriel K, Du W, Techner L, et al. A double-blind, randomized, placebo-controlled phase III study of the safety of alvimopan in patients who undergo simple total abdominal hysterectomy. Am J Obstet Gynecol 2006; 195: 445–53

[5] Nguyen DL, Maithel S, Nguyen ET, Bechtold ML. Does alvimopan enhance return of bowel function in laparoscopic gastrointestinal surgery? A meta-analysis. Ann Gastroenterol. 2015 Oct-Dec;28(4):475-80

[6] Wolff BG, Michelassi F, Gerkin TD, Techner L, Gabriel K, Due W, et al. Alvimopan, a Novel, Peripherally Acting μ Opioid Antagonist, Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase III Trial of Major Abdominal Surgery and Postoperative Ileus. Ann Surg 2004; 240: 728–735

[7] Adam MA, Lee LM, Kim J, Shenoi M, Mallipeddi M, Aziz H, et al. Alvimopan Provides Additional Improvement in Outcomes and Cost Savings in Enhanced Recovery Colorectal Surgery. Ann Surg 2016; 264: 141–146